Import and Export of Biological Products

CBER 101

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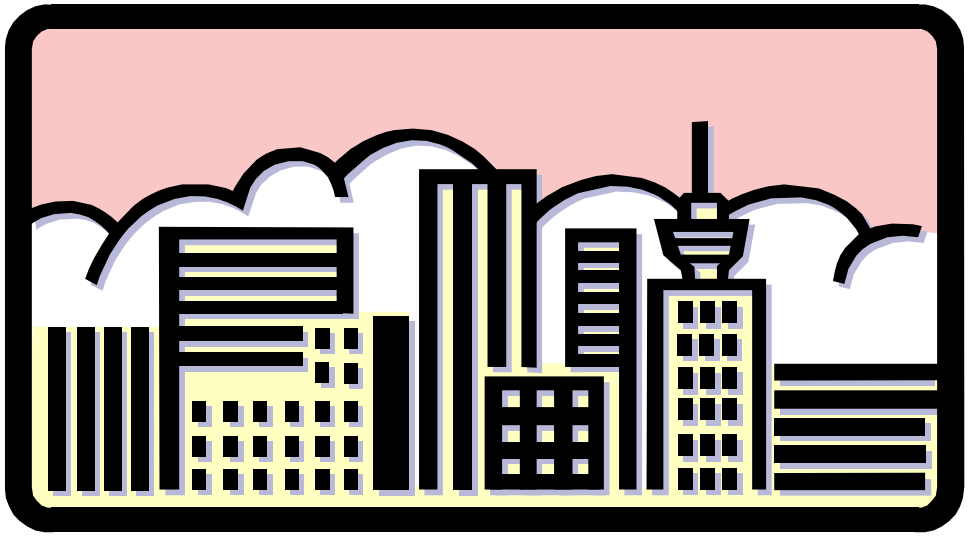
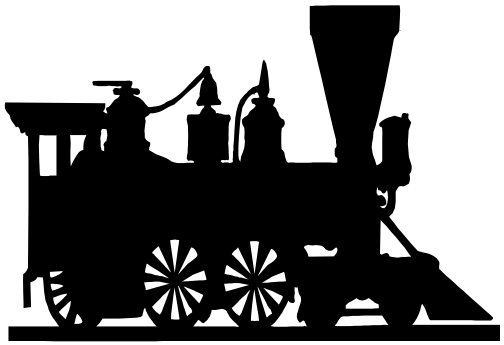
Objectives

- Import of Biological Products
- Import for export provisions
- Export of unapproved new human drugs and biologics
- Export of unapproved medical devices
- Export of partially processed biological products
- Certificates for export
- Export Reform

Imports





Import of Biological Products FD&C Act Section 801

- Biological Products may be imported provided:
  1. Made under cGMP
  2. Not forbidden in country of export and country of manufacturing
  3. Not adulterated, not misbranded, not violate FD&C Act, Section 505 (See Section 801(a))

  Secretary may authorize import for emergency medical care (See Section 801(d)(2))
- Import for Export (See Section 801(d)(3) and 801(d)(4))

Import of Clinical Investigational New Drug Products

Only new drugs for clinical investigational use with an active U.S. IND are authorized for importation

Import for Export

Section 801(d)(3)

Allows import of a component not in compliance if it is to be further processed by the initial owner or consignee or incorporated by the initial owner or consignee into a drug, biological product or device that will be exported under 801(e) or 802 of the FFDC Act, or Section 351(h) of the Public Health Service Act (PHS Act).

Import for Export

Requirements of initial owner or consignee importing:

1. Submit statement at the time of each importation
2. Must maintain records and
3. Export or destroy any unused imported component.

Bioterrorism Act of 2002

Bioterrorism Act of 2002 requires importers to:

- notification of intent to import (Register),
- Good and sufficient bond for product,
- identification of the manufacturer of the article along with any other entity that had possession of the article in the chain of possession from the manufacturer to the importer (Chain of possession), and
- Certificates of Analysis as necessary.

Bioterrorism Act of 2002 allows FDA to refuse admission if we determine that there is credible evidence or information indicating the article is not intended to be further processed or incorporated by the initial owner or consignee.

http://www.fda.gov/oc/bioterrorism/bioact.html

Import for Export of Blood, Blood components, Source Plasma, or Source Leukocytes

Section 801(d)(4)

- Importation must comply with PHS Act 351(a), or
- Comply with section 801(d)(3) and appropriate circumstances and conditions, as determined by FDA – submit request to CBER
- Tissue or a component or part of tissue is not permitted under this part of the Act, unless it complies with Section 361 of the PHS Act and 21 CFR 1270 &1271.

Section 801(d)(4)
Import for Export Request

Continued

For an import for export request to be approved for blood, blood components, source plasma or source leukocytes the following must be met:

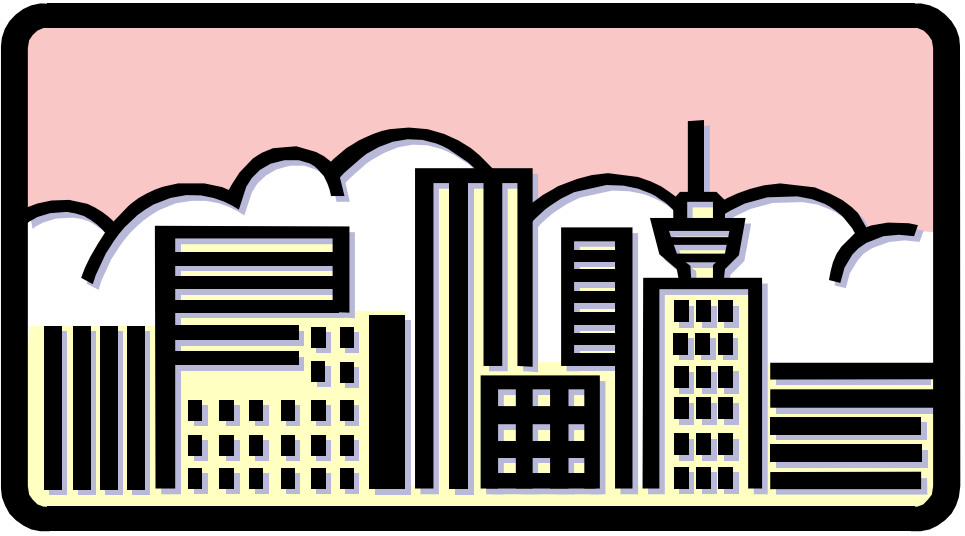
1. Information on the parties involved, what is being imported, and how it will be incorporated or further processed into a product for export;
2. The U.S. manufacturer “Should” register and list product for export;
3. Description of SOP’s to be implemented to ensure segregation of the imported product/material from U.S. approved products, and to prevent products developed from the imported product from being diverted;
4. Records of manufacturing, further processing, incorporation, or destruction, and records showing that all the requirements of the appropriate export mechanism have been met;
5. Evidence of an agreement between the U.S. manufacturer and the foreign supplier is strongly suggested;

Section 801(d)(4)
Import for Export Request

Continued

6. Labeling of imported material/product. Copies of labeling should be submitted in the import for export request and include the following:(a)Properly descriptive name; (b)Name and address of foreign manufacturer; (c) Donor, Lot, or Pool number; (d)Storage temperature; (e) Quantity; and (f) Statement: "Import for Export"; (g) Statement: "For Manufacturing Use Only" for injectable products, or "For Manufacturing into Non-injectable Products Only"; (h) Statement: "Not for Use in Products Subject to License under Section 351 of the Public Health Service Act.";(i) Statement that indicates whether or not the product has been tested for all infectious disease agents required and recommended by FDA; and (j) Appropriate biohazard labeling;
7. Donor Screening questionnaire - Translated into English; and
8. Specifications for the infectious disease testing and expected results.

Exports



Standard Export Requirements

Section 801(e)(1)

All products intended for export must:

- Accords to the specifications of the foreign purchaser
- Not be in conflict with the laws of the country to which it is intended for export
- Labeled on the outside of the shipping package to show it is intended for export
- Not been offered for sale or sold in domestic commerce

Export of Unapproved New Drugs and Biologics

Section 802(b)(1)(A)

Export of Unapproved Biological Products require:

1. Product must comply with importing country's laws.
2. Product must have marketing authorization in a listed country:
   - Australia
   - Canada
   - Israel
   - Japan
   - New Zealand
   - Switzerland
   - South Africa
   - European Union
   - EEA members

Export of Unapproved Medical Devices

Section 801(e)(2)

If your device does not have valid marketing authorization in a listed country [Section 802(b)(1)(A)], then an application to the HHS Secretary under Section 801(e)(2) may apply.

Export of Unlicensed Product to an Unlisted Country

Section 802(b)(2)

Request approval from the Secretary providing information that :

- the product complies with the laws of the importing country
- the product has valid marketing authorization by the appropriate authority in the importing country
- the foreign government of the importing country has certain statutory or regulatory standards:
  - review for safety and effectiveness
  - cGMP’s
  - Adverse event reporting and remove unsafe drugs from market
  - Label and promote as approved.

Export of Unapproved Biological Product

Section 802(b)(3)

Allows the petition for a product to be reviewed by the Secretary to allow export of the unapproved biological product to an unlisted country or when the product does not comply with other export mechanisms under the FD&C Act.

Petition under Section 802(b)(3)

Procedure to summit a petition for an unapproved product to an unlisted country:

1. Certify that the product does not comply with FDA or other listed country's conditions for product approval.
2. The manufacturer provides credible scientific evidence acceptable to the Secretary that the drug would be safe and effective under conditions of use in the country to which it is being exported.
3. Appropriate health authority in the country to which the drug is being exported can:
    a. request approval to export to such country
    b. certify that they understand that the drug is not approved by FDA or a listed country, and
    c. concurs that the credible scientific evidence provided to FDA for the drug is reasonably safe and effective.

The Secretary has 60 days to take action on this request.

Export of Unapproved New Investigational Biological Products

Section 802(c)

A drug or device intended for investigational use in a **listed** country may be exported in accordance with the laws of that country and shall be exempt from regulation under section 505(i) and 520(g). It is subject only to general conditions of 802(f), recordkeeping requirements of 802(g), and 801(e)(1). Notification to or approval by FDA is not required.

Export of Unapproved Clinical Investigational New Drug Products

21 CRF 312.110(b) allows the export of unapproved clinical investigational new drug products provided:

1. It complies with the active U.S. IND application and complies with 21 CFR 312.40
2. FDA authorizes shipment of the drug for clinical investigation. Authorization is requested by the exporting company or the importing government. Request is sent to the International Affairs Staff in the FDA.

Export of Unapproved New Drugs and Biologics

Section 802(d)

Export to fill pipeline

- Unapproved products may be exported to a listed country to fill pipeline in anticipation of marketing approval in that country

Section 802(e)

Export for tropical and low prevalence diseases

- Application filed with FDA for review and approval.

Export of Unapproved New Drugs and Biologics

Section 802(f)

Conditions include

- Substantial conformity with GMPs (or FDA-recognized international standards)
- Not otherwise adulterated
- Requirements of 801(e)(1)
- Not an imminent hazard
- Labeled with requirements and conditions for use
  - In the country where it received valid marketing authorization, and
  - In the country to which it is to be exported, and
  - In the language and units of measurement to which it would be exported or language designated by such country
- Promoted as labeled

Export of Unapproved New Drugs and Biologics

Section 802(g)

Simple notification to FDA when begin to export including:

(1) drug/device name and

(2) importing country as listed country(s) or the specific country name (if unlisted)

Record-keeping includes:

- Marketing authorization
- Distribution records
- Labeling used

Export of Partially Processed Biological Products

Section 351(h)

Export of Partially Processed Biological Products are permitted provided:

1. Product conforms with GMP or international manufacturing standards, and
2. Meets the requirements of Section 801(e)(1)

Export Certificates

- Section 801(e)(4) of FD&C Act authorizes FDA to issue certificate for human drugs (including biologics) and for devices within 20 days of a written request. FDA may charge a fee if the certificate is issued within 20 days.
- FDA Compliance Policy Guide Certification for Export (CPG 7150.01) allows for each Center to establish its own internal procedures for an exporter to request certificates.

Types of Export Certificates Issued by CBER

- Certificate to Foreign Government
- Certificate of Exportability (802)
- Certificate of Exportability (801)
- Certificate of Pharmaceutical Product (WHO Format)
- Non-clinical Research Use Only Certificate

FDA Export Reform and Enhancement Act of 1996

- FEDERAL REGISTER Draft FDA Guidance for Industry on: Exports and Imports Under the FDA Export Reform and Enhancement Act of 1996 – February 1998, Website address: http://www.fda.gov/ohrms/dockets/98fr/061298a.pdf
- (Draft Guidance for Industry on: Exports and Imports Under the FDA Export Reform and Enhancement Act of 1996 –guidelines and contacts

  http://www.fda.gov/opacom/fedregister/frexport.html

Export Reform

- FEDERAL REGISTER Import and Export; Reporting and Recordkeeping Requirements for Unapproved or Violative Products Imported for Further Processing or Incorporation and Subsequent Export;, Website address:

  http://www.fda.gov/ohrms/dockets/98fr/112498a.pdf

  and withdrawn see the Final Rule Stay 051402

  http://www.fda.gov/cber/rules/exportnotifstay.pdf
- FEDERAL REGISTER: Investigational New Drugs: Export Requirements for Unapproved New Drugs; Proposed Rule – 6/19/02